Axon guidance cues secreted by the cortex glial niche regulate asymmetric stem cell division in *Drosophila* larval brain neuroblast lineages

Ana de Torres-Jurado, Ana Carmena

Instituto de Neurociencias-CSIC/UMH, Alicante, Spain

Asymmetric stem cell division (ASCD) regulation is crucial to balance stem and differentiated cells during development, adult tissue homeostasis and tumorigenesis. Two main types of mechanisms, extrinsic and intrinsic, modulate ASCD. Extrinsic mechanisms include the secreted cues provided by the niche, a complex extracellular microenvironment surrounding stem cells that is essential for their maintenance. Intriguingly, ASCD in neuroblasts (NBs), the neural stem cells of *Drosophila* CNS and a paradigm for ASCD analysis, seems to depend exclusively on intrinsic cues, the so-called cell-fate determinants. Larval brain NB lineages are in close contact with the cortex glia, which enwraps each lineage individually providing neuroprotective and trophic functions. Thus, the cortex glia niche stands as an excellent candidate to be a source of secreted signals for regulating larval NB ASCD, but these potential signals remain elusive. Here we unravel a novel function for Slit and Netrin axon guidance cues as secreted signals by the cortex glial niche regulating larval brain NB ASCD through Robo and Frazzled (DCC-like) receptors, respectively. Slit and Netrins are present in the cortex glia while Robo and Frazzled are detected within NB lineages. Compromising Slit/Robo or Netrin/Frazzled signaling leads to ectopic NBs within the mutant clones suggesting a reversion of the daughter cell normally committed to differentiate to an NB, stem-like fate. Moreover, Slit/Robo signaling downregulation disrupts ASCD, reflected in defects in ASCD regulator and cell-fate determinant localization in mitotic NBs. We are currently investigating the mechanism/s by which these signaling cues impinge on NB ASCD.